

SUPPORTING INFORMATION

Synthesis of $[1',2',3',4',5',6'-^{13}\text{C}_6]\text{-(2',3',4',6'-Tetraacetyl-}\beta\text{-D-glucopyranosyl)-[6-}^{13}\text{C,1,3,4-}^{15}\text{N}_3\text{]-cytosine}$. To the suspension of $[6-^{13}\text{C,1,3,4-}^{15}\text{N}_3]\text{-N}^4\text{-benzoylcytosine}$ [9] (1.10 g, 5 mmol) and $[^{13}\text{C}_6]\text{-(glucosepenta-O-acetate}$ [11] (2.07 g, 5.3 mmol) in dichloromethane (20 mL) BSA (2.45 mL, 10 mmol) was added. The mixture was stirred under nitrogen at ambient temperature for 20 min to result a clear, colorless solution. After addition of SnCl_4 (1.76 mL, 15 mmol) under nitrogen the reaction mixture was heated under reflux for 2 h. The resulted brown mixture was cooled to ambient temperature, after removal of the solvent in vacuo the resulted oil was diluted in ethylacetate (100 mL) and washed with NaHCO_3 (75 mL). The voluminous precipitate of Sn(OH)_4 was filtered off and washed with ethylacetate (EE)(5 x 20 mL). The combined organic layers were washed with brine (2 x 50 mL) and dried over Na_2SO_4 . After evaporating the solvent the resulted oil was purified by column chromatography (silica, 14 x 3 cm, ethyl acetate / n-hexane = 2 : 1). Yield: 3.6 g (94 %); Rf (ethyl acetate): 0.48; mp: 247-249°C (methanol); 0.34; mp: 153 – 155°C (EtOH); $^{13}\text{C-NMR}$ (50 MHz, CDCl_3): δ = 20.2, 20.3, 20.4, 20.6 (4 x CH_3 Ac), 61.5 (d, J = 43 Hz, $\text{CH6}'$), 67.8 (t, J = 43 Hz, $\text{CH4}'$), 71.9 (t, J = 43 Hz, $\text{CH2}'$), 73.4 (t, J = 43 Hz, $\text{CH3}'$), 75.1 (t, J = 43 Hz, $\text{CH5}'$), 81.0 (d x d, J^1 = 14.6 Hz, J^2 = 45 Hz, $\text{CH1}'$), 94.7 (J_{NC} = 267 Hz, 5-C), 127.6 (3,5-CH Bz), 129.1 (2,6-CH Bz), 133.4 (4-CH Bz), 139.4 (J_{NC} = 48.5, 1-C Bz), 144.2 (J_{NC} = 48.4, 6-C), 155.2 ((t), J_{NC} = 11 Hz, 2-C), 164.7 (d, J_{NC} = 55 Hz, 4-C), 162.7 (C=O Bz), 169.5, 169.6, 169.8, 170.5 (4 x C=O Ac); $^{15}\text{N-NMR}$ (50 MHz, DMSO-d_6): δ = 100.5 (N4), 140.6 (N1), 235.0 (N3); Exact Mass: $\text{C}_{25}\text{H}_{28}\text{N}_3\text{O}_{11}$; Calc.: 556.1869; Found: 556.1862.

$[1',2',3',4',5',6'-^{13}\text{C}_6]\text{-(}\beta\text{-D-Glucopyranosyl)-[6-}^{13}\text{C,1,3,4-}^{15}\text{N}_3\text{]-cytosine}$. Yield: 2.50 g 92 %; Rf (ethyl acetate) 0.1, mp: 195-196°C (CH_2Cl_2); $^{13}\text{C-NMR}$ (50 MHz, DMSO-d_6): δ = 61.0 (d, J = 43 Hz, $\text{CH6}'$), 69.9 (t, J = 43 Hz, $\text{CH4}'$), 71.2 (t, J = 43 Hz, $\text{CH2}'$), 77.5 (t, J = 43 Hz, $\text{CH3}'$), 80.0 (t, J = 43 Hz, $\text{CH5}'$), 82.7 (d x d, J^1 = 14.6 Hz, J^2 = 45 Hz, $\text{CH1}'$), 92.0 (J_{NC} = 267 Hz, 5-C), 142.1 (J_{NC} = 48.4, 6-C), 155.5 ((t), J_{NC} = 11 Hz, 2-C), 165.5 (d, J_{NC} = 55 Hz, 4-C); $^{15}\text{N-NMR}$ (50 MHz, DMSO-d_6): δ = 91.8 (N4), 149.3 (N1), 212.5208.1 (N3); Exact Mass: $\text{C}_3\text{C}_7\text{H}_{30}\text{N}_2\text{O}_8$; Calc.: 284.1055; Found: 284.1061.

Synthesis of N^4 -Benzoyl-[1',2',3',4',5',6'- $^{13}\text{C}_6$]-(β -D-glucopyranosyl)-[6- ^{13}C ,1,3,4- $^{15}\text{N}_3$]-cytosine.

In an inert atmosphere TMSCl (1.80 g, 2 mL, 16 mmol) was added to a solution of [1',2',3',4',5',6'- $^{13}\text{C}_6$]-(β -D-glucopyranosyl)-[6- ^{13}C ,1,3,4- $^{15}\text{N}_3$]-cytosine (0.85 g, 3.2 mmol) in pyridine (8 mL). The mixture was stirred at ambient temperature for 15 min. After addition of benzoylchloride (0.91 g, 0.76 mL, 6.4 mmol) stirring was continued for another 3 h. The reaction mixture was cooled to 0 °C, ice water (10 mL) was added and after stirring for 15 min conc. NH_3 (20 mL) was added. The solvent was removed in *vacuo* after stirring for another 30 min at ambient temperature. The resulted oil was diluted with ethylacetate (EE) (100 mL) and washed with water (20 mL). After drying the organic layer over Na_2SO_4 the solvent was evaporated and the resulted oil was treated with MeOH /water (1 : 1, 14 mL) and ammonium chloride (2 g). After stirring the mixture at 40 °C for 4 hours, the solvent was evaporated to dryness, the residue was purified by column chromatography (silica, 24 x 3 cm, $\text{CH}_2\text{Cl}_2/\text{MeOH}$ = 9 : 1). Yield: 1.04 g (90 %); Rf (ethyl acetate) 0.52, mp: 189-191°C (CH_2Cl_2); ^{13}C -NMR (50 MHz, $\text{DMSO}-d_6$): δ = 59.0 (d, J = 43 Hz, $\text{CH6}'$), 67.9 (t, J = 43 Hz, $\text{CH4}'$), 69.8 (t, J = 43 Hz, $\text{CH2}'$), 75.4 (t, J = 43 Hz, $\text{CH3}'$), 78.6 (t, J = 43 Hz, $\text{CH5}'$), 82.6 (d x d, J^1 = 14.6 Hz, J^2 = 45 Hz, $\text{CH1}'$), 95.0 (d x d, J^1 = 14.6 Hz, J^2 = 66 Hz, 5-CH), 126.9 (3,5-CH Bz), 127.6 (2,6-CH Bz), 131.2 (4-CH Bz), 132.6 (J_{NC} = 48.5, 1-C Bz), 139.6 (d, J = 14.6 Hz, 6-CH), 147.7 ((t), J = 11 Hz, 2-C), 166.0 (d, J = 11 Hz, 4-C); Exact Mass: $\text{C}_{10}^*\text{C}_7\text{H}_{20}^*\text{N}_3\text{O}_7$; Calc.: 388.1447; Found: 388.1490.

6'-O-Monomethoxytrityl- N^4 -benzoyl-[1',2',3',4', 5',6'- $^{13}\text{C}_6$]-(β -D-glucopyranosyl)-[6- ^{13}C ,1,3,4- $^{15}\text{N}_3$]-cytosine. Yield: 2.27 g (83%); Rf ($\text{CH}_2\text{Cl}_2/\text{MeOH}$ = 9 : 1) 0.25, mp: 150 -154°C; ^{13}C -NMR (50 MHz, CDCl_3): δ = 54.8 (CH_3O), 62.6 (d, J = 43 Hz, $\text{CH6}'$), 69.7 (t, J = 43 Hz, $\text{CH4}'$), 73.6 (t, J = 43 Hz, $\text{CH2}'$), 76.3 (t, J = 43 Hz, $\text{CH3}'$), 77.6 (t, J = 43 Hz, $\text{CH5}'$), 82.8 (d x d, J^1 = 14.6 Hz, J^2 = 45 Hz, $\text{CH1}'$), 85.6 (C MMT), 97.5 (J_{NC} = 267 Hz, 5-C), 112.4 (AA'BB' MMT), 126.9 – 131.5 (C Ar MMT + Bz), 132.4 (4-CH Bz), 134.7 (1C-Bz), 136.3 (1C AA'BB' MMT), 143.7 (2 x 1C MMT), 144.2 (J_{NC} = 48.4, 6-C), 155.4 ((t), J = 11 Hz, 2-C), 157.9 (4C AA'BB'), 163.2 (C=O Bz), 166.6 (d, J = 11 Hz, 4-C);

¹⁵N-NMR (50 MHz, DMSO-d₆): δ = 96.7 (N4), 163.0 (N1), 224.9 (N3); Exact Mass: C₃₀*C₇H₃₆*N₃O₈:

Calc: 660.2648; Found: 660.2626.

[1',2',3',4',5'-¹³C₅]-5'-O-Monomethoxytrityl-*N*⁴-[6-¹³C, 1,3,4-¹⁵N₃]-benzoylcytidine dialdehyde.

Yield: 0.57 g (92 %); R_f (CH₂Cl₂/MeOH = 95 : 5) 0.49; MS: (LSIMS; Thgly, NaOAc; m/z (%): 273 (100 %) 662 (3) [M-H+2Na]⁺.

[1',2',3',4',5'-¹³C₅]-5'-O-Monomethoxytrityl-*N*⁴-[6-¹³C,1,3,4-¹⁵N₃]-benzoylcytidine [17]. Yield: 0.31 g (54 %); R_f (CH₂Cl₂/MeOH = 9 : 1) 0.38, mp: 140 – 146°C (CH₂Cl₂); ¹³C-NMR (50 MHz, DMSO-d₆): δ = 55.2 (s, CH₃O), 62.5 (d, *J* = 43 Hz, CH5'), 68.7 (t, *J* = 43 Hz, CH2'), 74.4 (d x d, *J* ~ 43 Hz, CH3'), 82.0 (d x d, *J* ~ 43 Hz, CH4'), 91.1 (d x d, *J*¹ = 12 Hz, *J*² = 45 Hz, CH1'), 85.6 (C MMT), 96.1 (*J*_{NC} = 267 Hz, 5-C), 113.0 (AA'BB' MMT), 126.9 – 131.5 (C Ar MMT + Bz), 132.9 (4-CH Bz), 133.4 (1C-Bz), 135.1 (1C AA'BB' MMT), 144.0 (2 x 1C MMT), 144.3 (*J*_{NC} = 48.4, 6-C), 154.5 ((t), *J* = 11 Hz, 2-C), 158.0 (4C AA'BB'), 163.2 (C=O Bz), 167.6 (d, *J* = 11 Hz, 4-C); Exact Mass: C₃₀*C₆H₃₄*N₃O₇:
Calc.: 629.2509; Found: 629.2527.